

REMARKS

Upon entry of the present amendment, claims 1, 12-15, and 29-30 are pending in the above-referenced patent application and are currently under examination. Claim 1 has been amended. Claim 30 has been newly added, no new matter has been introduced. Claims 8-11 have been newly canceled without prejudice to further prosecution. Reconsideration of the application is respectfully requested.

Claim 1 has been amended to recite a narrower genus, without prejudice to reintroduction or broader claims in a future application. Support for the amendments to the claim can be found in claim 1 as originally filed. Support for new claim 30 can be found in claim 1 as filed.

Applicants believe that the claim amendments add no new matter.

The claims 1 and 8-15 are rejected in various combinations under 35 U.S.C. § 112 and 35 U.S.C. § 103. In addition, claim 29 has been objected to. Each of these rejections and objections is addressed below in the order set forth by the Examiner.

I. INDEFINITENESS REJECTION

Claim 1 has been rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite. The Examiner alleges that when R⁶ is OR¹⁴, R¹⁴ being OP(O)(OR¹⁴)(OR¹⁴) is indefinite.

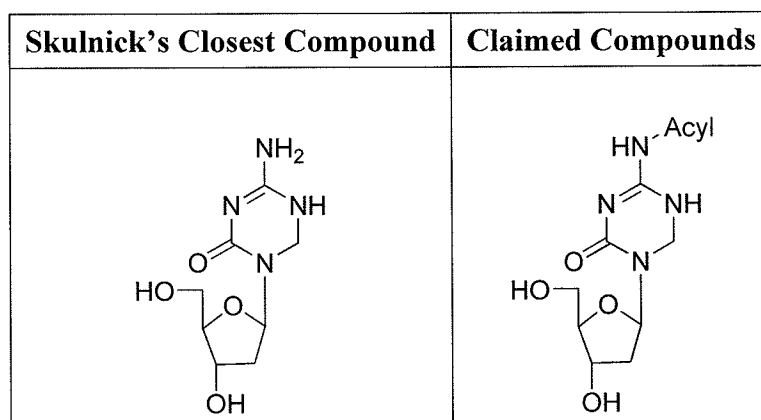
Applicants note that claim 1 has been amended to recite that R⁶ is -OH. In view of the current amendment, Applicants submit that the rejection is moot. Applicants request the Examiner to kindly withdraw the rejection.

II. OBVIOUSNESS REJECTION OVER SKULNICK

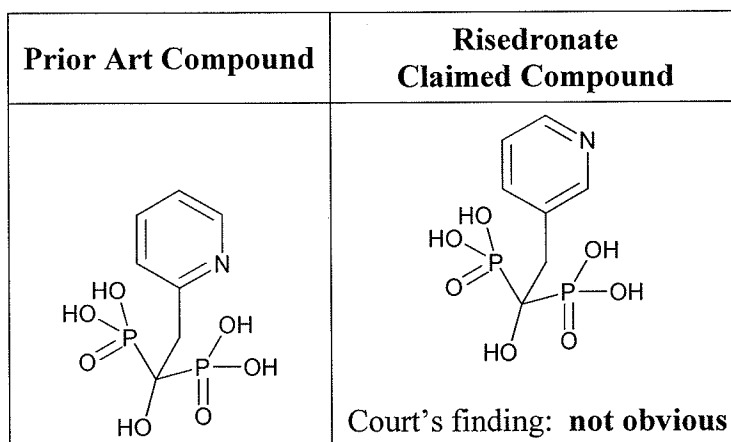
Claim 1 has been rejected under 35 U.S.C. § 103(a), as allegedly being obvious over Skulnick (U. S. Patent 4,171,431).

The Examiner alleges that because the Skulnick compounds and claimed compounds are very structurally similar, the motivation to make the claimed compounds can be found in the limitations of the compound generic of Skulnick. Applicants respectfully disagree because the unacylated compounds of Skulnick do not have sufficient structural similarity with the claimed acylated compounds to establish a prima facie case of obviousness, even with a teaching of (3,5-di-O-toluoyl-β-D-ribofuranosyl)-4-acetylimino compounds or acetyl functional groups in the generic disclosure.

The Examiner points to the following compound of Skulnick as being structurally similar to the claimed compounds and concludes that the instant claims are *prima facie* obvious because the claimed compounds are encompassed by the broad recitation of Skulnick. Applicants disagree because the claimed compounds do not have sufficient structural similarities to the Skulnick compounds to be *prima facie* obviousness.



The claimed compounds differ from Skulnick's closest compound by the presence of an acyl group on the N⁴-amine. The presence of the acyl group on the N⁴-amine alters the structure of the claimed compounds sufficiently that the claimed compounds are not *prima facie* obvious over the Skulnick compounds. In fact, the recent *Procter & Gamble* decision found that positional isomers, compounds having much greater structural similarity than for the claimed compounds and the Skulnick compounds, are not obvious¹:



¹ *Procter and Gamble Co. v. Teva Pharmaceuticals USA, Inc.*, Nos. 08-1404, -1405, -1406 (Fed. Cir. 2009)

Unlike the compounds of *Proctor & Gamble* which require no additional chemical moieties to modify the prior compound and arrive at the claimed compound, the Skulnick compounds must be *structurally modified* by addition of an acyl group in order to arrive at the claimed compounds. Thus, since the positional isomers of *Proctor & Gamble* are considered to be non-obvious, the structurally distinct claimed compounds are not obvious over Skulnick in the absence of motivation to modify the Skulnick compound with an acyl group.

The Examiner points to the 3',5'-di-O-toluoyl-N⁴-acyl compounds as motivation to select the acyl group. These compounds, however, describe N⁴-acyl groups in combination with 3',5'-di-O-toluoyl groups. Accordingly, the acyl-toluoyl compounds provide motivation for modification at 3 positions (3'-OH, 5'-OH and N⁴-amine) rather than a single substitution with an acyl group at the N⁴-amine. *Proctor & Gamble* considered this issue of the amount of variation required to achieve a successful result in the absence of any motivation for a particular substitution. *Proctor & Gamble* found that where the prior art provides "no indication of which parameters [are] critical or no direction as to which of many possible choices is likely to be successful," researchers can only "vary all parameters ... until one possibly arrive[s] at a successful result."²

In support of the Examiner's position, the Examiner alleges that the scope of compounds one of skill in the art would have to choose from is drastically reduced because only a single substitution is required to modify the Skulnick compound and arrive at the claimed compound. In making such an assertion, the Examiner appears to overlook the fact that while only a single change is required, making a single change in thousands of compounds still results in thousands of compounds. In fact, to arrive at a compound of current claim 1 by making a single change, one of skill in the art would have to select the starting compound, one of at least 10 positions to modify, and the substituent from the laundry list of substituents provided at column 2, lines 50-69 of Skulnick:

The X substituent is selected from the group consisting of oxygen, imino, lower-alkylimino, and lower-acylimino; R' is selected from the group consisting of hydrogen and loweralkyl; Y is selected from the group consisting of hydrogen, carboxacyl of from 1 through

18 carbon atoms, and phosphono; Y' is selected from the group consisting of carboxacyl and hydrogen; Z is selected from the group consisting of oxygen and sulfur; R is selected from the group consisting of hydrogen, lower-alkyl, phenyl, benzyl, cyclopropyl, lower-alkoxylower-alkyl, and lower-alkylthiolower-alkyl with the proviso that when R' is hydrogen, X and Z are oxygen, Y is hydrogen, carboxacyl of from 1 through 18 carbon atoms or phosphono, and Y'-O is in the erythro position, then R is hydrogen, lower alkyl of 2 through 4 carbon atoms, phenyl, benzyl, cyclopropyl, lower-alkoxylower-alkyl, or lower-alkylthiolower-alkyl; and pharmaceutically acceptable salts thereof when X is imino or lower-alkylimino or when Y is phosphono.

Because Skulnick has not identified the acyl group as a critical group from the many possible choices above, nor provided any direction for the modification of the N⁴-amine with an acyl group, one of skill in the art is left with the method described in *Proctor & Gamble*, “vary all parameters ... until one possibly arrive[s] at a successful result.” This is not sufficient to find a *prima facie* case of obviousness.

Accordingly, the obviousness rejection fails the test set forth in *Takeda*, finding that it is necessary to “identify some reason that would have led a chemist to modify a known compound in a particular manner” to find *prima facie* obviousness of a new claimed compound.³ Because the

² Id., p.10.

³ *Takeda Chem. Indus., Ltd. v. Alphapharm Pty., Ltd.*, 492 F.3d 1350, 1357 (Fed. Cir. 2007).

Examiner points merely to the 3',5'-di-O-toluoyl-N⁴-acyl compounds of Skulnick, and the broad recitation of substituents for the Skulnick compounds, the Examiner has not provided the necessary motivation to modify a compound, as required by *Takeda*.

Because the compounds and general disclosure of Skulnick fail to provide the necessary motivation to modify the compounds of Skulnick and arrive at the claimed compounds, the instantly amended claims are not obvious over Skulnick. Therefore, Applicants respectfully request that the Examiner withdraw the rejection.

III. OBVIOUSNESS REJECTION OVER SKULNICK AND FURTHER IN VIEW OF CULLIS

Claims 12-15 were rejected under 35 U.S.C. § 103(a), as allegedly being obvious over Skulnick (as applied for claim 1), and further in view of Cullis et al.

In view of the arguments submitted above, Applicants submit that Cullis does not remedy the deficiencies of Skulnick addressed above. Applicants request the Examiner to kindly withdraw the rejection for claims 12-15.

IV. OBVIOUSNESS REJECTIONS OVER SKULNICK AND FURTHER IN VIEW OF MCGUIGAN (REFERENCE U).

Claims 10-11 were rejected under 35 U.S.C. § 103(a), as allegedly being obvious over Skulnick (as applied for claim 1), and further in view of McGuigan *et al.* (reference U).

Applicants, without prejudice to further prosecution, have cancelled claims 10 and 11. In view of the cancellation this rejection is moot. Applicants request the Examiner to kindly withdraw the rejection for claims 10 and 11.

V. OBVIOUSNESS REJECTIONS OVER SKULNICK AND FURTHER IN VIEW OF MCGUIGAN (REFERENCE V).

Claims 8-9 were rejected under 35 U.S.C. § 103(a), as allegedly being obvious over Skulnick (as applied for claim 1), and further in view of McGuigan *et al.* (reference V).

Applicants, without prejudice to further prosecution, have cancelled claims 8 and 9. In view of the cancellation this rejection is moot. Applicants request the Examiner to kindly withdraw the rejection for claims 8 and 9.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance and an action to that end is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,



Alexander R. Trimble
Reg. No. 52,301

TOWNSEND and TOWNSEND and CREW LLP
Two Embarcadero Center, Eighth Floor
San Francisco, California 94111-3834
Tel: 415-576-0200
Fax: 415-576-0300
Attachments
ART:art
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